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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,182	10/19/2001	Michel Pairet	1/1244	5693

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EXAMINER
SHEIKH, HUMERA N

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/007,182	PAIRET ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,17-25 and 54-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,17-25 and 54-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Receipt of the Amendment filed 06/26/03 and the Information Disclosure Statement (IDS) filed 07/18/03 is acknowledged.

Claims 1-9, 17-25 and 54-56 are pending. Claims 1, 17-25, 54 and 55 have been amended. Claims 10-16 and 26-32 were cancelled. Claims 33-53, 57 and 58 were withdrawn. Claims 1-9, 17-25 and 54-56 remain rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9, 17-25 and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sarlikiotis et al. (US Pat. No. 6,284,287) in view of Garvey et al. (US Pat. No. 5,824,669).

Sarlikiotis teaches a pharmaceutical formulation for administration by inhalation, comprising a mixture of active compounds that include anticholinergics, such as atropine, atropine methonitrate, ipratropium bromide, oxitropium bromide and trospium chloride and antihistaminics, such as azelastine, flezelastine and methapyrilene (see abstract and col. 3, line 24 through col. 4, line 4). The active compounds can be employed as free bases, acids or as pharmaceutically tolerable salts. Counterions which can be employed are, for example, amines, bromide, chloride, iodide, carbonate, etc. (col. 3, lines 55-65).

The formulation, which can consist of a mixture of several finely ground active compounds, can also contain excipients, which have a mean particle size of 200-1000 microns. Suitable excipients are, for example, inorganic and organic salts, monosaccharides, such as *glucose* and its derivatives, disaccharides, such as *lactose, maltose and derivatives*, polysaccharides, such as starch and its derivatives and oligosaccharides, such as cyclodextrins. Mixtures of the auxiliaries can also be employed. The ratio of the active compound to the excipient material depends on the substances employed (see col. 3, line 65 through col. 4, line 25).

Sarlikiotis teaches anticholinergics, such as ipratropium bromide and is deficient only in the sense that he does not teach a tiotropium salt.

Garvey teaches pharmaceutical compositions for the treatment of respiratory disorders comprising therapeutically effective amounts of anticholinergic agents, such as atropine, ipratropium, flutropium, *tiotropium* and rispenzepine (see col. 2, line 12 through col. 6, line 55).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Garvey within the teachings of Sarlikiotis because Garvey teaches the use of tiotropium, ipratropium, etc. in the treatment of respiratory diseases and Sarlikiotis teaches the combination of an anticholinergic agent (i.e., ipratropium bromide) with an antihistamine. The expected result would be an improved tiotropium/antihistamine composition for treating respiratory disorders.

Claims 1-9, 17-25 and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvey et al. (US Pat. No. 5,824,669) in view of Naclerio (Clinical and Experimental Allergy-1998).

Garvey teaches pharmaceutical compositions for the treatment of respiratory disorders comprising therapeutically effective amounts of anticholinergic agents, such as atropine, ipratropium, flutropium, *tiotropium* and rispenzepine, wherein the compositions contain conventional excipients, such as *lactose* and amylose and are preferably administered by inhalation (oral and/or nasal) (see col. 2, line 12 through col. 6, line 55); (col. 28, lines 3-24).

Garvey is deficient in the sense that he does not teach the combined use of an anticholinergic with an antihistamine.

Naclerio teaches a study based on allergic rhinitis wherein the combination of an anticholinergic, such as ipratropium bromide combined with an antihistamine, can provide additional benefits, as compared to using the anticholinergic or anthistamine alone. The study suggests a synergistic effect can be obtained for the treatment of allergic rhinitis when both active ingredients are administered simultaneously (see pgs. 54-59).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made and one would be motivated to use the teachings of Naclerio within the teachings of Garvey because Naclerio teaches that a synergistic effect is obtained with the combined use of an anticholinergic and an antihistamine and Garvey teaches various anticholinergics that can be used which include, ipratropium and tiotropium as instantly claimed. The expected result would be an effective pharmaceutical formulation for respiratory-related diseases and disorders.

Claims 1-9, 17-25 and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naclerio (Clinical and Experimental Allergy-1998) in view of Garvey et al. (US Pat. No. 5,824,669) and further in view of Sarlikiotis et al. (US Pat. No. 6,284,287)

Naclerio teaches a study based on allergic rhinitis wherein the combination of an anticholinergic, ipratropium bromide combined with an antihistamine, can provide additional benefits, as compared to using the anticholinergic or anthistamine alone. The study suggests a synergistic effect can be obtained for the treatment of allergic rhinitis when both active ingredients are administered simultaneously (see pgs. 54-59).

Naclerio teaches the use of ipratropium bromide with an antihistamine and is lacking in the sense that he does not teach tiotropium.

Garvey teaches pharmaceutical compositions for the treatment of respiratory disorders comprising therapeutically effective amounts of anticholinergic agents, such as atropine, ipratropium, flutropium, *tiotropium* and rispenzepine, wherein the compositions contain conventional excipients, such as *lactose* and amylose and are preferably administered by inhalation (oral and/or nasal) (see col. 2, line 12 through col. 6, line 55); (col. 28, lines 3-24).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Garvey within the teachings of Naclerio because Garvey teaches the use of tiotropium, ipratropium, etc. in the treatment of respiratory diseases and similarly, Naclerio teaches a study based on allergic rhinitis wherein the combination of an anticholinergic, ipratropium bromide combined with an antihistamine, can provide additional benefits, as compared to using the anticholinergic or anthistamine alone. The expected result would be an effective

pharmaceutical formulation for the treatment of respiratory disorders, as similarly desired by the applicant.

Naclerio, as discussed above, teaches the use of ipratropium bromide with an antihistamine and is lacking in that he does not teach the instant excipients.

Sarlikiotis teaches a pharmaceutical formulation for administration by inhalation, comprising a *mixture of active compounds* that include *anticholinergics*, such as atropine, atropine methonitrate, ipratropium bromide, oxitropium bromide and trospium chloride and *antihistaminics*, such as azelastine, flezelastine and methapyrilene (see abstract and col. 3, line 24 through col. 4, line 4). The active compounds can be employed as free bases, acids or as pharmaceutically tolerable salts. The formulation, which can consist of a mixture of several finely ground active compounds, can also contain excipients, which have a mean particle size of 200-1000 microns. Suitable excipients are, for example, inorganic and organic salts, monosaccharides, such as *glucose* and its derivatives, disaccharides, such as *lactose, maltose and derivatives*, polysaccharides, such as starch and its derivatives and oligosaccharides, such as cyclodextrins.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the combined teachings of Sarlikiotis within Naclerio, because Sarlikiotis explicitly teaches a pharmaceutical formulation that comprises a mixture of active compounds, such as anticholinergics and antihistamines and that also comprises suitable excipients (i.e., glucose, lactose, maltose) and

similarly, Naclerio explicitly teaches a study based on allergic rhinitis wherein the combination of an anticholinergic (ipratropium bromide) combined with an antihistamine, can provide additional benefits, when compared to using the anticholinergic or anthistamine alone. The expected result would be an effective pharmaceutical formulation for the treatment of respiratory disorders, as similarly desired by the applicant.

Response to Arguments

Applicant's arguments filed 06/26/03 have been fully considered but they are not persuasive. The applicant stated, "Applicants have amended the claims and maintain that such amendments render the Examiner's rejections moot."

This argument has been thoroughly considered, but was not found to be persuasive. The examiner has now reformulated the rejections using the previously referenced art, based on the current amendments.

The instant claims are drawn to an inhalable powder pharmaceutical composition comprising a tiotropium salt, an antihistamine and a pharmaceutically acceptable excipient selected from glucose, arabinose, lactose, saccharose, or maltose, the tiotropium salt and the antihistamine optionally in the form of their enantiomers, mixtures of their enantiomers, their racemates, their solvates or their hydrates.

The prior art clearly teaches inhalable pharmaceutical formulations comprising mixtures of active compounds that contain anticholinergic agents in combination with antihistamines, whereby the compositions also contain suitable excipients (i.e., glucose, lactose, maltose) such as those instantly recited for the treatment of respiratory disorders. The prior art teaches similar ingredients for a similar intended purpose and in the same field of endeavor as the applicants. There is no significant distinction observed between the instant invention and the prior art, since Sarlikiotis, Garvey and Naclerio clearly meet all the instant claim limitation requirements. The applicants have not shown any surprising or unexpected results that accrue from the use of the instantly claimed ingredients. The prior art recognizes and achieves effective treatment methods for the treatment of respiratory disorders using the same active ingredients and excipients, as those instantly recited. Hence, the instant invention is rendered obvious and unpatentable over the prior art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (703) 308-4429. The examiner can normally be reached on Monday through Friday from 7:00A.M. to 4:30P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

hns
September 10, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600